Homology of the TetM with translational elongation factors: implications for potential modes of tetM conferred tetracycline resistance

Ray Sanchez-Pescador, Janice T.Brown<sup>1</sup>, Marilyn Roberts<sup>1</sup> and Mickey S.Urdea

Chiron Corporation, 4560 Horton St., Emeryville, CA 94608 and <sup>1</sup>Department of Pathobiology, SC-38, School of Public Health and Community Medicine, University of Washington, Seattle, WA 98195, USA Submitted November 16, 1987

the nucleotide sequence of tetM After our determination of isolated from Ureaplasma urealyticum (1), we searched by computer acid sequence coded by the analysis for homology of the amino largest open reading frame of our nucleotide sequence and the tetM gene reported from Streptococcus pneumoniae (2) against sequences in pDayhoff. The analysis revealed that the N-terminal a significant degree of homology with the region of TetM shares N-terminus offive diverse translational elongation factors. potential observations suggest roles for modulation of tetracycline sensitive cellular events.

Although most of the known tetracvcline resistance genes found in bacteria code for products involved in the active efflux of the antibiotic, the tetM determinant codes for a gene product apparently binds to ribosomes conferring tetracycline resistance to them both in vivo and in vitro (3). reasonable to propose that the homologous regions between the resistance factor and elongation factors constitute respective ribosome binding sites. Recent evidence indicates that tetracycline binds to the S7 protein of the 30S subunit ribosome (4). This event could presumably preclude the binding of aminoacvl-tRNA to the ribosome acceptor site thus blocking a result, translation. As two potential mechanisms by which the TetM acts are suggested. 1) The tetM gene product could bind to preventing tetracycline binding to the ribosome the S7 protein but permitting productive binding of the aminoacyl-tRNA. Whether or not tetracycline can bind or is bound to the ribosome in the presence ofthe tetM product remains t.o he determined. Alternatively, 2) TetM could act as a tetracycline resistant elongation factor. In this mode, the aminoacyl-tRNA could bind productively to the ribosome regardless of or in addition to tetracycline binding.

HEEROBELINIGVLANVONGETTLYESLLYNSGAITELGSVOGGTINTOWILJERGRGIT LOTGITSFOJENTEVNI IDJPGHEPLAEVYRSLSVLDGAILLISANDGVONYRI HSKEEUPERTRYNYNVOT GGYVHARTTLYBALT TVLAKTGGAMAAPDDIINGPEELAGIT INTSVETUTFTRHYMNYLCOHADYVSIGHITGANGEGALLVVANTDCHPDYTRE SYAAAFRISEPHYN 1071 GGYVHARTTLYBALTETLANGGAMELDYBAL - DRAFESBAGIT INTSVETETRIBHYSHYDCOGAMY INNII TGANGEGALLVVANTDCHPDYTRE HARGKERTERHIN 1071 GYVHARTTLYBALTHALANGH-GARRENGEDARAGIT INTSVETETRIBHYSHYDCOGAMYVNIGHITGANGEGALLVVSANDEPHDYTRE ARTTPIARTENIGISMIDAGRITTERILFYTOVGGIGGWEGGANTGANGGORGIT ISTANTTAPISGRARQYEPHRIN I I LUTPCHVEFNYRANYGEGOVANTETI RORYTD	TetM EF-Tu, <u>E.coli</u> EF-Tu, Yeast EF-Tu, Euglena EF-G, <u>E.coli</u>
MEEDBORII INIQVI.NYDAGETTI.TESILINGGA ITELGSVIRGT TRIINTI. LERGGITI.QTGITSPONENTKYNI IDTPONOPLAEVYRSI.SVI.GGAILI.ISAK MGKEKSHIWWYI.GWOGGESTTTGGLIYROGGIDKRI EKPEKEARELGKISFKYMWILKILARRERGITI.DIALMEPETPKYQYIVIDAPGBUPIDMITOTSONOCAILI INGG	TetM EF-1αA, Yeast
MEENBREI I NIGVLMYDAGRTTL/TESLLTNSGAITELGSVDKOTTRYUNTILERORGITIOTGITSPOMENTKYN I IDTPGHOUPLAEVYR SLSYLDGAILLI SA HAGREKIH INI WYLGYVDSGKETTTGFLI YKCGSIDKRTI EKPEKEAQENGKGSPKYMWLDKLKAERERGITID IALMEPETAKYYYT II DAPGHOP I KINI TOTSONDCAVLI VAA	TetM EF−1α, Shrimp

## References

- 1. Burdett, V. (1986) J. Bacteriol. 165, 564-569.
- 2. Sanchez-Pescador, R. et al., preceding paper.
- 3. Martin, P. et al. (1986) Nucleic Acids Res. 14, 7047-7058.
- 4. Goldman, R. et al. (1983) Biochemistry 22, 359-369.